UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/841,426 | 04/24/2001 | Jonathan W. Nyce | EPI-00311 | 5444 |

21971 7590 06/24/2005

WILSON SONSINI GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

| EXAMINER | |
|---|---|
| JIANG, SHAOJIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 06/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/841,426 | NYCE, JONATHAN W. | |
| | Examiner | Art Unit | |
| | Shaojia A. Jiang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15,17,29-31 and 36-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 17, 29-31, and 36-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



5.00

## DETAILED ACTION

This Office Action is in response to Applicant's amendment and response filed April 7, 2005 wherein claims 1-15, 17, 29-31, and 36-48 have been amended; claims 16, 18-28, 32-35, and 49-79 are cancelled previously.

Currently, claims 1-15, 17, 29-31, and 36-48 are pending in this application.

Claims 1-15, 17, 29-31, and 36-48 as amended now are examined on the merits herein.

Applicant's declaration Dr. Cynthia B. Robinson (not inventor), submitted April 7, 2005 under 37 CFR 1.132 is acknowledged and will be further discussed below.

The terminal disclaimer filed April 7, 2005, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. 5,527,789 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Therefore, the obviousness-type double patenting rejection as being unpatentable over U.S. 5,527,789 of record in the Final Office Action December 16, 2004 is withdrawn.

Applicant's amendment that amends claim 1, filed April 7, 2005 with respect to the rejection made under 35 U.S.C. 112 first paragraph for containing new matter, "**liquid** particles" of record stated in the Office Action dated December 16, 2004 has

been fully considered and is found persuasive to overcome the rejection since this recitation has been removed from the claims. Therefore, the said rejection is withdrawn.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15, 17, 29-31, and 36-48 as amended now are rejected under 35 U.S.C. 103(a) as being unpatentable Nyce (5,527,789, of record) in view of the book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6$^{th}$ Ed, page 454-455 for same reasons of record stated in the Office Action dated December 16, 2004.

Nyce discloses a pharmaceutical composition comprising the instant DHEA having the chemical formula (I) in a therapeutically effective amounts and the instant ubiquinone having the chemical formula (II) with n being from 1 to 12, 1 to 10, 6 to 10, or 10, in the therapeutically effective amounts, and a pharmaceutical carrier or diluent (see abstract, claims 13-19). Nyce also discloses the particular effective amounts of DHEA, i.e., 1-3600 mg/kg, 5-1800 mg/kg, or 20-100 mg/kg (see col.6 lines 6-7); and the particular effective amounts of ubiquinone, i.e., 1-1200 mg/kg, 30-600 mg/kg, or 50-150 mg/kg (see col.5 lines 64-66), within the instant claimed range, about 0.1-49% or about 1-20% w/w, since converting the known actual amount by actual weight to weight

percentage in a composition, w/w, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art. The pharmaceutical composition of Nyce further comprises a preservative, an antioxidant, a flavoring agent (e.g., sugar, see col.7 line 10), a buffering agent, a dispersant, or a surfactant (see col.6 line 67 to col.8 line 1, and col.7 lines 33-38) an inert base, glycerol (glycerin, see col.7 line 11-12). Nyce also discloses the instant forms of the formulation, e.g., nasal spay (see col.7 line 17) oral, rectal, topical, transdermal, nasal, or parenteral including injectable (see col.5 lines 37-41, col.6 lines 40-67), in a solution (an aqueous liquor), suspension.

Nyce does not expressly disclose the particular particles of the active agents having size herein, about 0.5-100 μm in size. Nyce does not expressly disclose employ a kit comprising the same composition.

The book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column). The text, "Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, teaches that the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the particles in the composition herein such as dehydroepiandrosterones and CoQn particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones and CoQn particles in range of size herein for nasal inhalation, since the nasal formulation or composition comprising two instant active agents is known based on Nyce. As discussed above, the book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column). The text, "Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, also teaches that the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column).

The teachings of these books clearly support that it is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

Further it would have been obvious to a person of ordinary skill in the art at the time the invention was made to put the same composition in to a kit because the employment of a known kit comprising a known pharmaceutical composition is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

***Response to Argument***

Applicant's arguments and Applicant's declaration of Dr. Cynthia B. Robinson, submitted April 7, 2005 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action December 16, 2004 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant primarily argues that "there is no "suggestion or motivation" in Nyce (5,527,789) or Ansel to combine these references. Particularly, these references do not teach the small particle size compositions of dehydroepiandrosterones or pharmaceutically or veterinarily acceptable salts thereof and ubiquinone". Applicant's argument is not found persuasive, as discussed in the previous Office Action, the nasal formulation or composition comprising two instant active agents is known based on Nyce.

More importantly, it must be recognized that any judgment on obviousness takes into account knowledge which was generally available and within the level of ordinary skill at the time the claimed invention was made. In this case, the book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6$^{th}$ Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column). The text, "Remington: The Science and Practice of Pharmacy", 20$^{th}$ Ed, by Alfonso R Gennaro, also teaches that the optimum size for inhalations is

known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column). Thus, the particle size for inhalations is well known in the art and generally available and within the level of ordinary skill at the time the claimed invention was made.

Therefore, the teachings of these books clearly support that it is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

Applicant's declaration of Dr. Cynthia B. Robinson (not inventor) under 37 CFR 1.132, has been fully considered but not found persuasive to rebut the prima facie case herein, since, first, even though the cited patent Nyce (5,527,789) is silent about the particle sizes, the same composition comprising the same compound for various administration forms including nasal inhalation administration is clearly taught; it is known that inhalations or nasal inhalation forms require the particle size, 0.5-0.7 μm or 0.5-5 μm as instantly claimed according to Reimgton's book or the book "Pharmaceutical Dosage Forms and Drug Delivery System". Thus, the particle size limitation would be inherently present in the nasal inhalation compositions of the prior art; thus, contrary to Applicant's assertion that "there is no reasonable expectation of success".

Second, the declaration provides no side-by-side comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art, i.e., comparing the particle size related to the testing results with the cited prior art.

Therefore, the declaration of Dr. Robinson is not persuasive to rebut the prima facie case herein.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15, 17, 29-31, and 36-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 159 of copending Application No. 10/072,010 for same reasons of record stated in the Office Action dated December 16, 2004.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the claim copending application and the claim of the instant application are drawn to the same composition comprising the dehydroepiandeosterone and ubiquinone, in particular, the particles of active having same size ranges.

Therefore, the claimed invention in claims 1-15, 17, 29-31, and 36-48 is clearly seen to be anticipated by claim 159 of copending Application No. 10/072,010.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In view of the rejections to the pending claims set forth above, no claims are allowed.

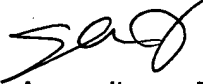
**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
June 13, 2005